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| 09/770,509 | 01/25/2001 | Fumiaki Katagiri | NADII.018A | 5860 |

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| EXAMINER | |
|---|---|
| VOGEL, NANCY S | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1636 | 20 |

DATE MAILED: 06/30/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/770,509 | KATAGIRI, FUMIAKI | |
| | Examiner | Art Unit | |
| | Nancy T. Vogel | 1636 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on 4/25/03 .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) 1-51 is/are pending in the application.

4a) Of the above claim(s) 3-5,7,8,11,14-16,18,19 and 22-51 is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1,2,6,9,10,12,13,17,20 and 21 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on 25 January 2001 is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 9&15 1/2 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

## DETAILED ACTION

This action is in response to the communication filed 25 April 2003.

Claims 1-51 are pending.

### *Election/Restrictions*

1. Applicant's election without traverse of Group I, claims 1, 2, 6, 9, 10, 12, 13, 17, 20, and 21 in Paper No. 18, filed 4/25/03, is acknowledged.

2. Claims 3-5, 7, 8, 11, 14-16, 18, 19, 22-51 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No.18.

### *Claim Rejections - 35 USC § 103*

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 2, 6, 12, 13 and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fueyo et al. (US Pat. No. 6,197,300) (A) in view of Desnottes (U).

Fueyo et al. disclose a method of identifying compounds having antimicrobial activity comprising the steps of (a) combining a polypeptide having substantial similarity to at least a portion of an oomycete FtsZ-mt protein SEQ ID NO: 2, and a compound to be tested for binding, [note the sequence comparison attached showing substantial similarity to at least a portion of oomycete FtsZ-mt1 (SEQ ID NO 1) in the Result 3 on the Sequence search results] (b) selecting a compound that binds to said protein (see columns 22-23 of the reference) and further states that the products from the first selection may be bacteriostatic or bacteriocidal (abstract and col. 22, lines 43-54). Fueyo et al. states that a goal of the methods disclosed is the use of the FtsZ polypeptide to screen for antimicrobials (see abstract).

The reference does not disclose the further steps of applying the compound of (b) to a microbe to test for antimicrobial activity, and selecting compounds that have antimicrobial activity.

Desnottes disclose methods for developing antimicrobial agents, comprising (a) combining a polypeptide involved in cell division, such as FtsZ, with a substance to be tested for interaction, (b) selecting those compounds that interfere with FtsZ function in a primary screen which may be mechanism-based or target-directed, (c) applying selected compounds from step (b) to microorganisms of interest and (d) testing for bacteriostatic or bacteriocidal activity (see Figure 1).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the method disclosed by Fueyo et al. to include a last step of in vitro testing for effectiveness, i.e. applying the compound from step (b) above

to a microbe, as taught by Desnottes, to test for antimicrobial activity, and to further select those compounds that possess such activity, since Fueyo et al. states that the FtsZ polypeptide is to be used to screen for antimicrobials, and since as taught by Desnottes, it was obvious to one of ordinary skill in the art at the time the invention was made to apply this second screening step of in vitro testing of antimicrobial activity for any compound being tested for use as a pharmaceutical.

One would have been motivated to test the effectiveness of any prospective antimicrobial directly against a microbe by the desire to confirm that a potential pharmaceutical agent is active against disease causing microbes.

***Claim Rejections - 35 USC § 112***

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1, 2, 6, 9, 10, 12, 13, 17, 20, 21 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The rejection is based on the Guidelines for the Examination of Patent Applications under the 35 U.S.C. 112, first paragraph "Written Description published in the Federal Register (Volume 66, Number 4, Pages 1099-1111). Claim 1 is drawn to a

method of identifying compounds having antimicrobial activity comprising combining a polypeptide having substantial similarity to at least a portion of an oomycete FtsZ-mt protein with a compound to be tested, and then identifying those compounds that have antimicrobial activity. Claim 2 specifies that the polypeptide is encoded by an isolated DNA comprising a nucleotide sequence, which is substantially similar or identical to at least a portion of the sequence ID NO:1. Claim 6 specifies that the polypeptide of claim 1 is substantially similar or identical to the amino acid sequence of SEQ ID NO:2. Claims 9 and 10 specify that in the method of claim 1, the microbe is an oomycete, or *Phytophthora infestans*, respectively. Claim 12 is drawn to a method of identifying an inhibitor of FtsZ-mt activity having antimicrobial activity comprising combining a polypeptide having substantial similarity to at least a portion of an oomycete FtsZ-mt protein, and a compound to be tested, and then identifying those compounds that bind to said polypeptide Claim 13 recites that the polypeptide of claim 12 is encoded by an isolated DNA comprising a nucleotide sequence which is substantially similar or identical to at least a portion of the sequence ID NO:1. Claim 17 recites that the polypeptide of claim 12 is substantially similar or identical to the amino acid sequence of SEQ ID NO:2. The specification has defined the term "substantially similar" as encompassing nucleotide sequences encoding polypeptides having substantially the same structure and function as the polypeptide encoded by the reference nucleotide sequence, and may be 65% percent similar (page 15 of the specification). The specification has defined the term "a portion" of a nucleic acid or polypeptide sequence, to refer to a substantially contiguous segment of adjacent nucleic acids or amino

acids...such that the segment is of sufficient length to encode or include a functional or active part or domain of a polypeptide, or a part of a polypeptide that is not functional or active...but which carries at least one other kind of useful feature..." (page 14 of the specification). Claims 1, 9, 10, 12, 20, and 21 are genus claims in terms of a method using any polypeptide having substantial similarity to a portion of an oomycete FtsZ-mt protein; the claims encompass a broad class of methods using a polypeptide that may be virtually any part of any oomycete FtsZ-mt, having 65% homology thereto. Claims 2 and 13 are genus claims in terms of a method using any polypeptide encoded by an isolated DNA comprising a nucleotide having substantial similarity to a portion of SEQ ID NO 1, and therefore the claims encompass a broad class of methods using a polypeptide that may be encoded by virtually any part of SEQ ID NO 1, having 65% homology thereto. Claims 6 and 17 are genus claims in terms of a method using a polypeptide that is substantially similar to the amino acid sequence of SEQ ID NO: 2, and therefore encompass methods using any polypeptides having at least 65% similarity to SEQ ID NO 2, and that still retain substantially the same structure and function as the native protein. The specification teaches the method using the full length oomycete FtsZ mt1 polypeptide. The disclosure is not deemed to be descriptive of the complete structure of a representative number of species encompassed by the claims as one of skill in the art cannot envision all the methods utilizing the encompassed polypeptides based on the teachings of the specification. While the specification provides general information on conserved regions of known FtsZ proteins, there is no disclosure of the precise amino acids useful for identifying compounds with antimicrobial

activity. Furthermore, there is no structure-function analysis of the disclosed oomycete FtsZ mt1 protein to provide guidance on the essential regions of the protein that could be modified and retain function. Therefore, the specification does not describe the claimed method utilizing peptides substantially similar to at least a portion of any oomycete FtsZ-mt in such full, clear, concise and exact terms so as to indicate that Applicant has possession of the method at the time of filing the present application. Thus, the written description requirement has not been satisfied.

7. Claim 12, and by dependence, claims 13, 17, 20 and 21 are drawn to a method of identifying an inhibitor of FtsZ-mt activity having antimicrobial activity, comprising combining a polypeptide having substantial similarity to at least a portion of an oomycete FtsZ-mt protein, and a compound to be tested for ability to inhibit an activity of said FtsZ-mt protein, under conditions conducive to such inhibition, and selecting a compound that is capable of inhibiting said FtsZ-mt activity. The disclosure is not deemed to be descriptive of this method, since there is no description of an assay for selecting for inhibition of any activity of FtsZ protein. Although the specification describes the bacterial FtsZ protein as being "a key component of the bacterial cell division machinery" (page 3 of the specification), and further describes that in bacteria FtsZ forms a filamentous ring at the site of cell division (page 3 of the specification), there is no disclosure of a precise method for selecting compounds that inhibit any FtsZ activity. Therefore, the specification does not describe the claimed method for identifying an inhibitor of FtsZ-mt activity having antimicrobial activity in such full, clear, concise and exact terms so as to indicate that Applicant had possession of the method

at the time of filing the present application. Thus the written description requirement has not been satisfied.

8. Claims 12, and by dependence, claims 13, 17, 20 and 21 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are directed to a method of identifying an inhibitor of FtsZ-mt activity having antimicrobial activity, comprising combining a polypeptide having substantial similarity to at least a portion of an oomycete FtsZ-mt protein, and a compound to be tested for ability to inhibit an activity of said FtsZ-mt protein, under conditions conducive to such inhibition, and selecting a compound that is capable of inhibiting said FtsZ-mt activity.

The following factors have been considered in formulating this rejection (*In re Wands*, 858F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988): the breadth of the claims, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, the amount of direction or guidance presented, the presence or absence of working examples of the invention and the quantity of experimentation necessary.

The present claims are very broad. Claims 12, 13, 17, 20 and 21 encompass a method for identifying an inhibitor of FtsZ-mt activity, using a polypeptide having

substantial similarity to at least a portion of any oomycete FtsZ-mt protein (claims 12, 20 and 21), or using a polypeptide encoded by DNA substantially similar to SEQ ID NO: 1 (claim 13), or using a polypeptide substantially similar or identical to SEQ ID NO: 2 (claim 17). Thus, the claims encompass methods using a virtually limitless number of possible polypeptides for the identification of inhibitors of FtsZ –mt activity.

The nature of the invention is a method of identifying inhibitors of any FtsZ-mt activity using the oomycete FtsZ-mt protein, or polypeptides having substantial similarity to at least a portion thereof.

An analysis of the prior art as of the effective filing date of the present application shows the lack of documented assays for the inhibition of FtsZ activity. In addition, there is no guidance in the prior art regarding structure function relationships for the FtsZ-mt proteins, and therefore one of ordinary skill in the art would have no idea which portions or which particular amino acids, are vital for the structure and function of the FtsZ-mt protein such that it can be used in the claimed method. Since the specification does not disclose an assay for inhibition of the FtsZ activity, one of ordinary skill in the art would not be able to identify which of the myriad of polypeptides encompassed by the claims would be useful for identifying inhibitors.

The relative skill of those in the art of genetic manipulation and rational drug discovery is high.

The area of the invention is unpredictable. It is well known that one cannot predict, from an amino acid sequence alone, which regions and/or amino acids will, when isolated or altered, result in a polypeptide that retains a desired activity.

Berendsen (V) discusses the difficulty of predicting any protein structure from a known sequence, stating that "one of the 'grand challenges' of high-performance computing – predicting the structure of proteins—acquires much of the flavor of the Holy Grail quest of the legendary knights of King Arthur: It is extremely desirable to possess but extremely elusive to obtain" (page 6).

The present specification provides little or no guidance to support the claimed invention for a method of identifying inhibitors of FtsZ-mt. There is no method for assaying inhibition of FtsZ-mt function disclosed, and there is no guidance regarding which regions of FtsZ-mt may be altered and still retain the function needed for use in the recited method.

There are no working examples of a method of identifying inhibitors of FtsZ-mt in the specification. In addition, there are no working examples of the isolation of a portion of the FtsZ-mt that retains function, or of other alterations to the protein that retain the function necessary for the necessary for use in the recited method.

The quantity of experimentation necessary to carry out the claimed invention is high, as the skilled artisan could not rely on the prior art or the present specification to teach how to use the claimed methods. In order to determine how to practice the claimed invention, one of skill in the art would have to design and implement an assay for the inhibition of FtsZ-mt activity. In addition, one would have to identify regions and amino acids of the FtsZ-mt protein which when isolated or altered, respectively, would result in a polypeptide that retained activity in the claimed method. Since neither the

prior art nor the specification provides appropriate guidance in these matters, it would require a large quantity of unpredictable experimentation by the skilled artisan to do so.

Based on the broad scope of the claims, the unpredictability in the area of the invention, the lack of sufficient guidance or working examples in the specification and the quantity of experimentation necessary, it would clearly require undue experimentation by one of skill in the art to determine how to make and/or use the claimed method of identifying inhibitors of the FtsZ-mt activity.

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 2, 6, 9, 10, 12, 13, 17, 20, 21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 12, and by dependence, claims 2, 6, 9, 13, 17, 20, 21 are indefinite in their recitation of "substantial similarity to at least a portion". This term is not defined by the claims and the specification does not provide a standard for ascertaining the requisite degree, therefore one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Claim 12 and by dependence claims 13, 17, 20 and 21 are indefinite in the recitation of "an activity". It is not clear what activity is intended.

***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nancy T. Vogel whose telephone number is (703) 308-4548. The examiner can normally be reached on 7:30 - 4:00, Monday - Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Irem Yucel, Ph.D. can be reached on (703) 305-1998. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-3014 for regular communications and (703) 305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

ntv
June 27, 2003

TERRY MCKELVEY
PRIMARY EXAMINER